Postgrad Med J 1995; **71**: 186–188 © The Fellowship of Postgraduate Medicine, 1995

Letters to the Editor

Cerebellar ataxia in coeliac disease – no evidence of a humoral aetiology

Sir,

Many patients with dermatitis herpetiformis also have a small bowel enteropathy which responds to withdrawal of gluten from the diet. However, in this setting, coeliac disease is usually mild and rarely results in clinical malabsorption. Both disorders have a high association with HLA, B8 and DR3 antigens and are suspected to have, at least in part, an immune pathogenesis. Some 10% of patients with coeliac disease develop neurological complications (box). Cook[1] compiled a series of 16 patients and drew attention to the fact that these were the same neurological disorders that occur in paraneoplastic disease.

Paraneoplastic cerebellar ataxia is most frequently associated with small cell lung cancer or carcinoma of the breast or ovary. Patients with breast or ovarian carcinoma have high titres of an IgG directed against a cytoplasmic antigen in cerebellar Purkinje cells.[2] Whether this antibody is involved in the pathogenesis of the disorder or simply a epiphenomenon is not yet clear. The aetiology of cerebellar ataxia found with coeliac disease is equally obscure although vitamin deficiency, particularly of vitamin E, does not appear to be relevant.[3] We were interested to look for the presence of an anti-Purkinje cell antibody in a patient with coeliac disease and anti-Purkinje cell antibody in a patient with coeliac disease and cerebellar ataxia.

Our patient was a 65-year-old caucasian woman who presented with a 12-month history of progressive unsteadiness of gait and slurring of speech. She had a past history of reversible airways disease, dermatitis herpetiformis and, two years prior to her neurological presentation, had been found to have coeliac disease. Despite having no symptoms of malabsorption, investigations had revealed an abnormal xylose tolerance test (1 h plasma xylose 0.69 mmol/l; normal range 0.65–1.35 mmol/l), positive antigliaden and endomysial antibody and severe villous atrophy of the small bowel. She had been unable to tolerate a gluten-free diet. She smoked 10 cigarettes per day and she did not drink alcohol. At the time of investigation she was taking Becotide and salbutamol inhalers. There was no family history of note.

General medical examination was normal. She had a cerebellar dysarthria, normal external ocular movements and an ataxia of limb and gait. Deep tendon reflexes were preserved, plantar responses flexor, and there were no sensory signs.

Neurological complications of coeliac disease

- peripheral neuropathy
- myelopathy
- brain stem encephalitis
- cerebral ataxia
- Lambert – Eaton myaesthenic syndrome

Investigations revealed normal haematological and biochemical indices, thyroid function, B12, folate and chest X-ray. Wasserman reaction and autoantibodies were negative. Antigliaden IgG and antiendomysial IgA antibody were positive. CT scan and the cerebrospinal fluid (CSF) were normal in all respects; no oligoclonal bands were detected. Serum vitamin E and vitamin E/lipid ratio were normal.

Using an indirect immunofluorescence technique serum and CSF was screened for activity against human and rat cerebellar Purkinje cells and dorsal root ganglia neurones. No activity was found. Normal controls, sera from patients with other neurological diseases, and positive controls were also examined.

In Cook's original series[1] of 16 patients, three were found to have ataxia. Most also had a polyneuropathy so it is difficult to be certain whether the gait disturbance was entirely cerebellar. However, the majority of post-mortem examinations in this and other series[4,5] demonstrated Purkinje cell loss and a variable depopulation of the neurones in the granular layer and dentate nuclei. Subsequent reports[3–6] whilst confirming the clinical association, have failed to cast any light on the aetiology. A dysimmune hypothesis is attractive – in both coeliac and paraneoplastic disease there is an increased incidence of B8 and DR3 antigens, and several syndromes may co-exist in the same patient. Some disorders occur in both autoimmune disease and in association with malignancy, eg, Lambert-Eaton myaesthenic syndrome (LEMS). In LEMS the antibody has been shown to be responsible for the clinical syndrome.

At least in this patient we have failed to demonstrate any anti-Purkinje cell activity and a humoral aetiology remains unproven.

DJ DICK
D ABRAHAM
Norfolk & Norwich Hospital, Brunswick Road, Norwich, Norfolk, NR1 3SR, UK
G FALKOUS
Muscular Dystrophy Laboratories, Newcastle General Hospital, Westgate Road, Newcastle-Upon-Tyne NE4 6BE, UK
S HISHON
James Paget Hospital, Lowestoft Road, Gorleston, Great Yarmouth, Norwich NR31 6LA, UK

We thank Dr JB Pilling for his permission to report this case.

1 Cook WT, Smith T. Neurological disorders associated with adult coeliac disease. *Brain* 1966; **89**: 638–722.
2 Jaeckle KA, Graus F, Houghton A, Cardon-Cardo C, Nielson SL, Posner JB. Autoimmune response of patients with a paraneoplastic cerebellar degeneration to a Purkinje cell cytoplasmic protein antigen. *Ann Neurol* 1985; **18**: 592–600.
3 Ward ME, Murphy JT, Greenberg GR. Celiac disease and spinocerebellar degeneraton with normal vitamin E status. *Neurology* 1985; **35**: 1199–201.
4 Finelli PF, McEntee WJ, Ambler M, Kestenbaum D. Adult coeliac disease presenting as a cerebellar syndrome. *Neurology* 1980; **30**: 245–9.
5 Kinney HC, Burger PC, Hurwitz BJ, Hijmans JC, Grant JP. Degeneration of the central nervous system associated with coeliac disease. *J Neurol Sci* 1982; **53**: 9–22.
6 Hermaszewski RA, Rigby S, Dalgleish AG. Coeliac disease presenting with cerebellar degeneration. *Postgrad Med J* 1991; **67**: 1023–4.

Delayed severe rhabdomyolysis after taking 'ecstasy'

Sir,

A previously fit 36-year-old man was admitted in the early hours of New Year's Day following a convulsion at a night club. According to friends he had taken one 'ecstasy' tablet, two bottles of beer and a large quantity of water during the night. On admission his axillary temperature was 36.2°C and his Glasgow coma score was 3/15. His pupils were equal and reactive to light and he had no focal neurological abnormalities.

Shortly after admission, he had two further convulsions, was incontinent of urine, vomited several times and became restless. Chest X-ray showed abnormal shadowing in the left lung field. Blood tests revealed a serum sodium concentration (Na^+) of 115 mmol/l (normal 137–144 mmol/l) and a creatine kinase (CK) of 1572 IU/l (<250 IU/l); potassium, urea and creatinine were normal. His arterial pH was 7.5 with an oxygen saturation of 97% on air. He also had a raised white cell count (14.6×10^9/l) with a neutrophil leucocytosis. Clotting studies and liver function tests were normal. Further tests revealed serum 3,4-methylenedioxymethamphetamine (MDMA) levels of 0.013 mg/l with both MDMA and its metabolite 3,4-methylenedioxyamphetamine in his urine. Treatment was with diazepam and chlorpromazine for the fits and agitation and co-amoxyclav and hydrocortisone for a presumed aspiration pneumonia. Intravenous hydration was commenced with 11 of twice normal saline over 12 h, and a nasogastric tube passed.

Twelve hours after admission the patient remained comatose. His respiratory rate had risen to 32/min, his oxygen saturation had dropped to 90% on air and he had developed an axillary pyrexia of 39°C. He had also become polyuric, passing 5 l of urine since admission. Repeat biochemistry showed a serum Na^+ of 120 mmol/l with a CK of 2461 IU/l. His plasma osmolality was 259 mmol/kg (275–285 mmol/kg) with a urine osmolality of 153 mmol/kg (50–1400 mmol/kg) and a urine Na^+ of 26 mmol/l. CT brain scan was normal. He received oxygen, and paracetamol for his pyrexia which peaked at 39.7°C (axilla).

Eighteen hours after admission his temperature started to fall and his level of consciousness began to improve. By 30 h after admission his serum Na^+ was 132 mmol/l with a plasma osmolality of 278 mmol/kg. However his CK had risen to 81900 IU/l with an alanine aminotransferase (ALT) concentration of 132 IU/l (<34 IU/l). He had also become oliguric – passing 250 ml of urine in nine hours. His urine tested positive for myoglobin.

He was treated aggressively with a forced alkaline diuresis induced by intravenous

Side effects of ecstasy

- hyperpyrexia
- rhabdomyolysis
- renal failure
- hyponatraemia
- convulsions
- death

fluids, mannitol, bicarbonate and low dose dopamine. His CK peaked at 84 800 IU/l some 48 h after admission with an ALT of 239 IU/l. By that time, he had regained full consciousness but remembered nothing of the previous two days. His only complaint was of aching arms and legs. His CK returned to near normal levels (1444 IU/l) over the next four days; his ALT peaked at 323 IU/l five days after admission, by which time myoglobinuria was no longer present. Throughout the admission his serum potassium, urea and creatinine did not rise above normal levels.

Severe rhabdomyolysis and myoglobinuria has mostly been reported as an early phenomenon in patients admitted with hyperpyrexia following 'ecstasy' ingestion.[1,2] Our patient's temperature did not rise until nine hours after admission (and then perhaps due to pneumonia) and remained elevated for only 18 hours. His CK rose substantially 30 h after admission, the minor rise on the first day being ascribed initially to his three convulsions. It seems likely that this was a delayed response to his pyrexia, although we are not aware of any previous reports of such massively raised CK levels (84 800 IU/l) following 'ecstasy' ingestion – despite higher temperatures having been observed.[3]

The possibility of missing such delayed, severe rhabdomyolysis in similar cases needs to be borne in mind. As in our case, vigorous treatment of rhabdomyolysis can prevent renal damage.[4]

In contrast to the cases reported by Maxwell and colleagues,[5] hyponatraemia in our patient was probably dilutional, arising from the large quantity of water imbibed, rather than due to the syndrome of inappropriate antidiuretic hormone secretion; both plasma and urine osmolalities were low. Large volumes of water are commonly drunk with 'ecstasy' as prophylaxis against dehydration and heat exhaustion during dancing.

The serum level of MDMA found in our patient would generally be regarded as non-toxic (toxicity $>$ 0.2 mg/l). Evidently, severe consequences may occur in the setting of prolonged physical activity even at MDMA levels far below this. Our patient had taken 'ecstasy' once previously without ill effects, but previous experience with the drug clearly gives no guarantee of safety.

We thank our clinical colleagues for their help in the management of this patient, and the Poisons Unit, Guy's Hospital, London for measuring MDMA levels.

ED LEHMANN
CH THOM
DN CROFT
St Thomas' Hospital, London SE1 7EH, UK

1 Screaton GR, Singer M, Cairns HS, Thrasher A, Sarner M, Cohen SL. Hyperpyrexia and rhabdomyolysis after MDMA ('ecstasy') abuse. *Lancet* 1992; **339:** 677–8.
2 Henry JA, Jeffreys KJ, Dawling S. Toxicity and deaths from 3,4-methylenedioxymethamphetamine ('ecstasy'). *Lancet* 1992; **340:** 384–7.
3 Chadwick IS, Curry PD, Linsley A, Freemont AJ, Doran B. Ecstasy, 3-4 methylenedioxymethamphetamine (MDMA), a fatality associated with coagulopathy and hyperthermia. *JR Soc Med* 1991; **84:** 371.
4 Fahal IF, Sallomi DF, Yaqoob M, Bell GM. Acute renal failure after ecstasy. *BMJ* 1992; **305:** 29.
5 Maxwell DL, Polkey MI, Henry JA. Hyponatraemia and catatonic stupor after taking 'ecstasy'. *BMJ* 1993; **307:** 1399.

Pseudohyperkalaemia associated with hereditary spherocytosis

Sir,

Alani *et al* reported a case of hereditary spherocytosis complicated by thromboembolism, with typical perfusion defects on lung scanning.[1] In such a case, the differential diagnosis would include alternative causes of multiple perfusion defects, such as *in situ* thrombosis in the pulmonary circulation. The latter was the postulated cause of pulmonary hypertension in the patient with hereditary spherocytosis reported by Verresen *et al*,[2] who suggested that the pathogenesis was sequestration of erythrocytes in the pulmonary microcirculation, due to poor deformability resulting from spectrin deficiency.[3] This hypothesis owes its credibility to the fact that poor deformability of erythrocytes has been validated as the underlying mechanism in the pathogenesis of pulmonary hypertension complicating sickle cell disease.[4]

OMP JOLOBE
Department of Medicine for the Elderly, Tameside General Hospital, Lancashire OL6 9RW, UK

1 Alani FSS, Dyer T, Hindle E *et al*. Pseudohyperkalaemia associated with hereditary spherocytosis in four members of a family. *Postgrad Med J* 1994; **70:** 749–51.
2 Verresen D, de Backer W, von Meerbeeck J *et al*. Spherocytosis and pulmonary hypertension. Coincidental occurrence or causal relationship? *Eur Respir J* 1991; **4:** 629–31.
3 Lux SE, Becker PS. Disorders of the red cell membrane skeleton: hereditary spherocytosis and hereditary elliptocytosis. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. *The metabolic basis of inherited disease*. 6th edn. New York, NY: McGraw-Hill, 1989, pp 2367–2408.
4 de Gruchy GC. The sickle haemoglobinopathies. In: Penington D, Rush B, Castaldi P, eds. *Clinical haematology in medical practice*. 4th edn. Oxford: Blackwell, 1978, pp 286–98.

Intestinal cytomegalovirus infection: a diagnostic problem in an HIV-positive patient

Sir,

Unexplained abdominal pain may be a problem in patients with AIDS. We report a 30-year-old woman infected with human immunodeficiency virus (HIV) through sexual contact about three years previously, who presented with intermittent generalised abdominal discomfort. Examination was initially unremarkable and an abdominal X-ray showed her to have severe faecal retention but treatment with laxatives failed to relieve pain. Her CD4 lymphocyte count was 0.065×10^9/l (range 0.5–1.5).

During the following three months a series of investigations yielded normal results: these included sigmoidoscopy, rectal biopsy, upper abdominal and pelvic ultrasonography, MRI abdominal scan and barium studies of the small and large bowel. Stool microscopy and culture failed to reveal relevant pathogens. Cultures for cytomegalovirus (CMV) were sterile in rectal biopsy, urine, throat swabs and blood. She had IgG antibody to CMV indicative of infection at some time but titres were static and CMV IgM was not detected by immunofluorescence or enzyme immunoassay. The pain responded to symptomatic treatment but diffuse abdominal tenderness persisted. She remained afebrile throughout. Three months after presentation she unexpectedly collapsed and died. At post-mortem there was peritonitis and patchy ileal inflammation with a mid ileal perforation. The colon appeared normal macroscopically and histologically: examination of the inflamed ileal tissue showed changes diagnostic of CMV infection.

Features of CMV infection of the gut in HIV patients

- bowel perforation
- necrotising enterocolitis
- appendicitis

The investigation of abdominal pain in patients with HIV infection is often influenced by the site of pain and the presence or absence of diarrhoea[1]; a diagnosis can be reached in most patients.

CMV infection of the gut is well recognised in AIDS patients (box).[2–4] In our patient there was no pain localisation or other feature to suggest CMV; indeed CMV seemed to have been excluded. In patients in whom intestinal CMV infection has caused perforation, the site is usually between the distal ileum and splenic flexure[5] and colonoscopy, which was not performed in our patient, would be preferable to sigmoidoscopy to discover affected gut mucosa (colonoscopy would have been normal in this patient).

This case highlights the fact that intestinal CMV infection may be difficult, indeed impossible, to diagnose without invasive investigation such as laparoscopy or laparotomy. Because ganciclovir may be effective in CMV colitis[6] and may benefit patients with CMV ileitis, we conclude that a diagnostic trial of anti-CMV treatment may have a role to play in CMV antibody positive AIDS patients with persisting abdominal pain of uncertain cause despite appropriate investigations.

RBS LAING
PHILIP D WELSBY
Regional Infectious Disease Unit, City Hospital, Edinburgh EH10 5SB, UK

1 Thuluvath PJ, Connolly GM, Forbes A, Gazzard BG. Abdominal pain in HIV infection. *Q J Med* 1991; **78:** 275–85.
2 Frank D, Raicht RF. Intestinal perforation associated with cytomegalovirus infection in patients with acquired immune deficiency syndrome. *Am J Gastroenterol* 1984; **79:** 201–5.
3 Horner PJ, Tanner AG, Clarke DM *et al*. Necrotizing enterocolitis in a patient with AIDS. *AIDS* 1992; **6:** 737–51.
4 Dieterich DT, Kim MH, McMeeding A, Rotterdam H. Cytomegalovirus appendicitis in a patient with acquired immune deficiency syndrome. *Am J Gastroenterol* 1991; **86:** 904–6.
5 Kram HB, Shoemaker WC. Intestinal perforation due to cytomegalovirus infection in patients with AIDS. *Dis Colon Rectum* 1990; **30:** 1037–40.
6 Dieterich DT, Kotler DP, Busch DF. Ganciclovir treatment of cytomegalovirus colitis in AIDS: a randomised, double-blind, placebo-controlled multicenter study. *J Infect Dis* 1993; **167:** 278–82.